REMARKS

Claims 1-69 are currently pending in the application. Claims 28-66 are withdrawn. Claims 6, 23, and 26 are amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

The specification has been amended to delete the Abstract on page 976. The Abstract on page 201 is the correct Abstract.

Claim Objections

The Office Action states that claims 1-27 and 67-69 are objected to on the grounds that the recitation, "a second amino acid sequence comprising a ligand for a cell surface polypeptide of a leukocyte," is awkwardly presented. The Office Action suggests amendment to, "a second amino acid sequence comprising the amino acid sequence of a ligand for a cell surface polypeptide of a leukocyte."

The claim is intended to limit the second amino acid sequence to being capable of binding to the recited cell surface polypeptide (whether or not the entire second amino acid sequence is required for such binding). Applicants are uncertain as to how the proposed amendment renders the claim language less awkward. Applicants respectfully request further explanation from Examiner regarding this language. Pending such explanation and/or discussion, Applicants respectfully maintain the language as originally entered.

Rejection of Claims 6-14, 23, and 26 Under 35 U.S.C. §112, Second Paragraph

The Office Action states that claims 6-14, 23, and 26 are rejected for indefiniteness under 35 U.S.C. §112, second paragraph. The Office Action states that the claims are rejected on the grounds that the recitation "at least about", particularly the word "about", renders the claim indefinite. Applicants respectfully disagree. Nevertheless, in order to expedite prosecution, Applicants are herewith amending claims 6, 23, and 26 to remove the word "about".

Rejection of Claims 23 and 26 Under 35 U.S.C. §112, First Paragraph

The Office Action states that claims 23 and 26 are rejected under 35 U.S.C. §112, first paragraph, on the grounds that it fails to comply with the written description requirement. In particular, the Office Action objects to the recited limitation that the second amino acid sequence comprise at least five contiguous amino acids of a naturally occurring GM-CSF. The Office Action states that this limitation is directed at a genus, and further states that Applicants fail to provide adequate written description of the genus by providing sufficient description of a representative number of species. Applicants traverse the rejection.

First, Applicants note that the Office Action states, "... the cytokine is the active component that provides the adjuvant activity. Thus, the claim is drawn encompass [sic] second amino acid sequence having at least five contiguous amino acids of a naturally occurring GM-CSF, and function as an adjuvant." This statement imputes function to the second amino acid sequence that is not a requirement of the invention, i.e. what is claimed. Indeed, Applicants submit that it is the entire multifunctional molecule of the invention that is responsible for any improved and unexpected "adjuvant" effect. The latter point aside, though, the second amino acid sequence is defined in the claim **not** by any self-contained adjuvant activity, but rather by the ability to bind to a cell surface polypeptide of a leukocyte, as recited in independent claim 1. In addition, it is well settled that, although claims are read in light of the specification, limitations from the specification may not be read into the claims, where the claims are not so narrowly drawn. *In re Prater*, 415 F.2d 1393, 1404-05 (CCPA 1969). In the instant case, the rejection stated in the Office Action is based on an improper reading of a functional limitation into the claims. The recited functional limitation relating to the second amino acid sequence is that the second amino acid sequence is able to bind to a cell surface polypeptide or a leukocyte. The arguments in the Office Action regarding written description are, therefore, not proper or relevant, to the extent that they rely on an impermissible reading of a functional limitation (adjuvant activity) into the claim.

The Office Action states that the specification does not provide the complete structure of naturally occurring GM-CSF. In fact, the specification provides references that teach the full amino acid sequence of GM-CSF (see paragraph 0157).

Furthermore, the specification teaches that the second amino acid sequence preferably includes at least five contiguous amino acids of a cytokine (see paragraph 0008), and more specifically teaches the preferred embodiment wherein the second amino acid sequence comprises at least five contiguous amino acids of naturally occurring GM-CSF (see paragraph 0052).

The Office Action acknowledges that adequate written description can rest on disclosure of relevant identifying characteristics, and sets forth a number of specific means by which this approach can be perfected. For example, the Office Action states that written description can be satisfied by delineation of physical and/or chemical properties and functional characteristics. Applicants agree that such criteria can fulfill the written description requirement. In fact, there is a key functional and physical/chemical limitation in the claims that derives from the description in the specification. That is, that the second amino acid sequence must be a ligand for a cell surface polypeptide of a leukocyte. Applicants further note that there is extensive and well-known information in the literature regarding which amino acids of GM-CSF molecules are necessary and which are not necessary for receptor binding and/or bioactivity. See, for example, Shanafelt et al., 1991, J. Biol. Chem. 266: 13804; Shanafelt and Kastelein, 1989, PNAS 86: 4872; Hercus et al., 1994, Blood 83:3500; Altman and Kastelein, 1995, J. Biol. Chem. 270: 2233; Monfardini et al., 1996, J. Biol. Chem. 271: 2966; Lopez et al., 1992 EMBO 11: 909; Meropol et al., 1992 J. Biol. Chem. 267: 14266; Schanafelt and Kastelein, 1992 J. Biol. Chem., 267: 25466; Seelig et al., 1994, J. Biol. Chem. 269: 5548; Shanafelt et al., 1991, EMBO 10: 4105 (Exhibits A-J, respectively). Thus, one of ordinary skill in the art would easily discern many members of a genus from the disclosures of the instant specification, and would recognize that the inventors were, correspondingly, in possession of many such members.

The Office Action further states that, under the written description requirement, "The full compound is required," citing *Fiers v. Revel* and *Amgen v. Chugai*. The cited cases, however, dealt with subject matter and issues that are fundamentally different from those of the instant invention. Specifically, the claims at issue in both cited cases were aimed at DNA molecules, the sequences of which were entirely unknown to man and which were not disclosed in the relevant specifications. In both cases, the DNA molecules themselves were claimed on the basis

of encoding a given, complete polypeptide (human fibroblast beta interferon and human erythropoietin, respectively), even though the sequences of any such DNA's were not taught in the specifications and were unpublished by anyone at the time of filing. In other words, the DNA molecules were claimed in the absence of knowledge regarding their own, actual physical or chemical identities or properties.

The subject matter now at issue, i.e. the amino acid sequence comprising at least five contiguous amino acid molecules of naturally occurring GM-CSF, differs in at least two important ways from that of *Fiers* and *Amgen*. First, the amino acid sequences of GM-CSF are well-known in the art and are, indeed, provided by the instant specification. Second, the invention, i.e. what is claimed, is further defined by the fact that the "second amino acid sequence" can bind to a cell surface polypeptide of a leukocyte. Thus, unlike the claims of *Fiers* and *Amgen*, the instant claims define the metes and bounds of the claim element by its own structural and physical/chemical properties.

In addition, Applicants note that they were in full possession of the claimed invention at the time the application was filed. The species described fully embody all elements of the invention as claimed, and the specification therefore clearly conveys possession of the claimed invention to one skilled in the art. Applicants further note that the limitation regarding "at least five contiguous amino acids" is meant to exclude compositions failing to meet this standard, and that anyone reasonably skilled in the art could easily discern whether, on that basis, a given method fell within or without the potential purview of the claims in this regard.

Accordingly, Applicants respectfully request that Examiner withdraw the rejections under 35 USC 112, first paragraph.

Rejection of Claims 1, 2, 4-8, 15, 16, and 18-21, and 69Under 35 U.S.C. §102

The Office Action states that claims 1-2, 4-8, 15-16, 18-21, and 69 are rejected under §102 for lack of novelty over Ramshaw et al., U.S. Pat. No. 5,866,131. The Office Action states that Ramshaw et al. teaches a fusion polypeptide comprising a first amino acid sequence that can bind to a carbohydrate binding domain [sic], and a second amino acid sequence that is a ligand

for a cell surface polypeptide, particularly a cytokine receptor. The Office Action states further that the first amino acid sequence is the hemagglutinin protein, and that the second amino acid sequence includes the murine IL-2 protein, the murine TNF protein, and the murine IL-3 protein.

Applicants respectfully traverse the rejection.

Ramshaw et al., in fact, does not teach a fusion polypeptide at all. Although this reference teaches nucleic acid constructs that encode multiple amino acid sequences, they are expressed as separate molecules, rather than as a fusion polypeptide. This is expressly evident from the drawings of Ramshaw et al, especially Figure 6a. Moreover, Ramshaw et al. clearly states at column 7, lines 6-8, that the hemagglutinin and cytokine were coexpressed from the viral constructs, "but from separate sites in the viral genome." Thus, they are not combined in a fusion polypeptide.

In order to support a rejection under 35 U.S.C. §102, a reference must teach all elements of the claimed invention. Since a fusion polypeptide is an essential element of the claimed invention, and since Ramshaw et al fails to teach a fusion polypeptide, the '131 patent does not anticipate the instant claims.

Therefore, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection of Claim 3, 9-14, 17, 22-27, 67-68 Under 35 U.S.C. §103

The Office Action states that claim 3 is rejected under §103 as being obvious over Ramshaw et al, discussed above, in view of Meyers et al, U.S. Pat. No. 6,911,317. Applicants traverse the rejection.

As discussed above, Ramshaw et al. does not teach the fusion polypeptide recited in claim 1. There is no teaching in Meyers et al. to supplement the deficient teachings of Ramshaw et al. Accordingly, even if combined, the references cited to not teach each element of the clamed invention. Furthermore, given their widely disparate teachings, there would have been

no motivation to combine these references, nor is it clear how they could be combined to yield the teachings of the instant invention.

The Office Action also states that claims 9-14 are rejected as being obvious over Ramshaw et al. in view of Fiers et al., US20030129197. Applicants traverse the rejection.

Again, as discussed above, Ramshaw et al. does not teach the fusion polypeptide recited in claim 1. There is no teaching in Fiers et al. to supplement the deficient teachings of Ramshaw et al. Accordingly, even if combined, the references cited to not teach each element of the clamed invention.

The Office Action also states that claim 17 is rejected as being obvious over Ramshaw et al., that claims 22-27 are rejected as being obvious over Ramshaw et al. in view of Wortham et al., and that claims 67-68 are rejected as being obvious over Ramshaw et al. in view of Natesan, U.S. Pat. No. 6,015,709. Applicants traverse the rejections.

In each case, as above, Ramshaw et al. does not teach the fusion polypeptide recited in claim 1, and the rejected claims each depend directly or indirectly from claim 1. There is no teaching in the secondary references to supplement the deficient teachings of Ramshaw et al. Accordingly, even if combined, the references cited to not teach each element of the clamed invention.

Accordingly, Applicants request that the rejections be reconsidered and withdrawn.

Double Patenting

The Office Action states that the instant claims are rejected under the judicially created doctrine of obviousness type double patenting in view of several co-pending applications. Upon notification of allowable subject matter in the instant case, Applicants will timely file a terminal disclaimer effective to obviate the double patenting rejection.

Applicants submit that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with

Applicants' attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

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